Remarks

The Office Action dated November 6, 2002 has been carefully reviewed and the foregoing amendments are made in response thereto. In view of these amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants respectfully submit that no new prohibited matter has been introduced by the amendments. Written description support for the substitute claims can be found throughout the specification and in the original claims.

Summary of the Office Action

1. Claims 1, 3 and 6-9 were rejected under 35 U.S.C. 112 (second paragraph).

2. Claims 1, 3 and 6-11 were rejected under 35 U.S.C. 112 (first paragraph) for lack of written description in the specification.

3. Claims 1, 3 and 6-11 were rejected under 35 U.S.C. 112 (first paragraph) for lack of enablement by the specification.

4. Claims 1, 3, 6-8 and 10-11 were rejected under 35 U.S.C. 102(a) as being anticipated Molloy *et al.* (1997) Electrophoresis 18, 2811-2815.

Rejection Under 35 U.S.C. 112 (second paragraph)

Claims 1, 3 and 6-9 were rejected under 35 U.S.C. 112 (second paragraph) purportedly because claims 1 and 3 are missing a step of how to analyze or detect the presence of a protein comprising SEQ ID NO: 3 in a tear sample. Applicants have cancelled these claims therefore the rejection is moot. In light of substitute claims 15-27, however, Applicants submit that the substitute claims, when viewed in light of the specification, disclose all that is necessary for the skilled artisan to detect a protein having a molecular weight of about 10 kiloDaltons and a pI of about 5.1 in a tear sample from an animal. For example, beginning on page 4, line 01 through page 5, line 21 the specification discloses preparation of the tear sample for detection of the protein, and subsequent detection of the protein by molecular weight determination by two-dimensional gel electrophoresis. Furthermore, the skilled artisan could readily determine the molecular weight and pI of the protein in these claims using any equivalent means available in the field of the invention.

Rejections Under 35 U.S.C. 112 (first paragraph)

The Office Action rejected claims 1, 3 and 6-11 under 35 U.S.C. 112 (first paragraph) as containing subject matter which lacks proper written description. The basis of this rejection appears to be the purported lack of specific disclosure of a sufficient number of representative examples of the claimed genus of a protein having an N-terminal sequence comprising SEQ ID NO: 3. Respectfully, for the sole purpose of furthering prosecution, Applicants have cancelled these claims without prejudice, therefore the rejection is moot. In view of substitute claims 15-29, however, Applicants respectfully submit that these substitute claims find sufficient written description in the as-filed specification.

The substitute claims refer expressly to a protein having a molecular weight of about 10 kiloDaltons, a pI of about 5.1 and with regard to claim 29, an N-terminal sequence comprising SEQ ID NO: 3. The Office Action asserts that the canceled claims were drawn to a large genus of proteins and that the claims are not supported by a representative number of fully described species (see Office Action at page 5, lines 8-11). Applicants submit that substitute claims 15-27 are drawn to a method of detecting a small subgenus of proteins with the recited physical properties, and with regard to claim 29, an N-terminal sequence comprising SEQ ID NO: 3. The skilled artisan could readily identify any of these proteins using the methods exemplified in the specification (*e.g.*, two-dimensional gel electropheresis with isoelectric focusing (IEF) in the first phase as set forth on the specification on pages 4-5) to identify the presence of a protein with a pI of about 5 and a molecular weight of about 10 kiloDaltons. With regard to claim 29, the specification discloses N-terminal sequencing of a protein with these physical properties on page 5, lines 22-25. Applicants therefore submit that the substitute claims are drawn to detection of a small subgenus of proteins, all of which exhibit the properties specified in these claims and that undue experimentation would not be encountered by the ordinary skilled artisan in the execution of the detection step for this small subgenus of proteins.

The Office Action also stated that the specification provided adequate written description for a method of screening for, or detecting cancer, in an animal, comprising obtaining and detecting in a tear sample the presence of the amino acid sequence consisting of SEQ ID NO: 3. Applicants respectfully disagree because a protein consisting of the amino acid sequence SEQ ID NO: 3 was never isolated, rather the full-length protein was isolated and only its N-terminous was sequenced to reveal the amino acid sequence of SEQ ID NO: 3. Furthermore, it is not possible for a protein with a sequence consisting of SEQ ID NO: 3 to have a molecular weight of about 10 kiloDaltons because there simply are not enough amino acids present, regardless of the different types of amino acids in SEQ ID NO: 3, to result in

a protein with this molecular weight.

Claims 1, 3 & 6-11 were also rejected under 35 U.S.C. 112 (first paragraph) purportedly because the specification does not enable the skilled artisan to use the invention commensurate in scope with these claims. Applicants have cancelled these claims without prejudice or disclaimer and replaced them with substitute claims 15-29. In light of substitute claims, however, Applicants respectfully submit that these claims are commensurate in scope with the disclosure of the specification.

The Office Action asserts that the specification does not reasonably provide enablement for an antibody against a specific protein epitope having an N-terminal sequence comprising SEQ ID NO: 3 because the structure of the epitopes are not disclosed in the specification. The Office Action further states that without disclosure of specific epitopes, the genus of antibodies that bind "specifically" or "selectively" to SEQ ID NO: 3 would also detect unrelated proteins. Applicants have amended the claims such that the claimed method requires that the protein be identified by its physical characteristics (*e.g.*, molecular weight and its isoelectric point). Applicants submit that it is not necessary for an antibody to specifically or selectively bind to a protein with a molecular weight of about 10 kiloDaltons, a pI of about 5.1 and optionally, having an N-terminal sequence comprising SEQ ID NO: 3 in order to detect the presence of this protein.

The specification discloses two-dimensional gel electrophoresis to isolate and identify from tears a protein with the molecular weight of about 10 kiloDaltons, a pI of about 5.1 and a N-terminal sequence comprising SEQ ID NO: 3 (see "Methods" section on pages 4-5). Applicants therefore submit that the specification discloses all that is necessary to practice the claimed method of substitute claim 15 because it discloses sample preparation from a tear and detection of a protein with the aforementioned features using separation methods well known to the skilled artisan. It is therefore not necessary to detect the protein using a labeled probe. Thus, the features of the substitute claim 15 no longer requires detection by an antibody.

Nonetheless, the skilled artisan could readily use a labeled probe such as an antibody as set forth in claim 21 to detect the presence of the protein. For example, by employing a Western blot assay, the skilled artisan could detect the presence of the protein using an antibody which binds both to a protein having an N-terminal sequence comprising SEQ ID NO: 3 and to other unrelated proteins because the physical properties of the protein would be sufficient to identify its presence. Detection by an antibody is now an optional step in the substitute claims which confirms the presence of the protein having an N-terminal sequence comprising SEQ ID NO: 3. Furthermore, Applicants submit that it would be routine

for the skilled artisan to prepare an antibody which binds to a protein having an N-terminal sequence comprising SEQ ID NO: 3. The Office Action also indicates that it would be routine to make an antibody which bound to a protein having an N-terminal sequence comprising SEQ ID NO: 3 (see Office Action at page 8, line 5).

Rejection Under 35 U.S.C. 102(a)

Claims 1, 3, 5-8 and 10-11 were rejected under 35 U.S.C. 102(a) as being anticipated Molloy *et al.* (1997) Electrophoresis 18, 2811-2815. In response to the Examiner's request in the Office Action dated November 6, 2002 Applicants are in the process of obtaining a certified copy of the priority application (Australian application PO 5009) and respectfully request that the rejection be held in abeyance until such time that the certified copy of the priority application is submitted in a supplemental amendment. The certified copy of the priority application will clearly provide the necessary evidence to antedate the Molloy *et al.* reference.

OK

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, he is invited to telephone the undersigned at his convenience.

If there are any other filing or claim fees due in connection with the filing of this amendment, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for any extension of time under 37 C.F.R. 1.136 not accounted for above, such an extension is requested and the fee should be charged to our Deposit Account.

Respectfully submitted,
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Dated: **May 6, 2003**
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